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REMARKS

Claims 5-8, 11, 22-24, 29, 30, 40-48 and 51-54 presently appear in this case. Claims 22, 29, 30, and 40-43 have been withdrawn from consideration. No claims have been allowed. The official action of January 15, 2004, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to DNA encoding a polypeptide which potentiates cell death and has the sequence of SEQ ID NO: 1, as well as analogs and fragments thereof. The invention also relates to vectors and host cells containing the DNA, polypeptides encoded by the DNA, and methods of producing the polypeptides using such a host cell, as well as the pharmaceutical compositions. The present invention is also directed to oligonucleotide molecules consisting of an antisense sequence of at least a part of an mRNA encoding a polypeptide of the present invention and a pharmaceutical composition containing such oligonucleotide. The invention further relates to a method of use of the DNA and polypeptides for modulating the effect of the B1 protein on the activity of inflammation or cell death or cell survival pathways or any other signaling activity.

The examiner states that the present application contains claims drawn to an invention non-elected with

traverse, and that a complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action. A Petition under 37 C.F.R. § 1.144 was filed on March 26, 2004. This is "other appropriate action" with respect to the non-elected claims. Thus, it is not necessary to delete the non-elected claims until a final decision has been received with respect to the petition.

The examiner states that claim 54 is dependent from a rejected claim, although the examiner has interpreted it as being intended to have been dependent from claim 44.

Claim 54 has now been amended to confirm that it is intended to be dependent from claim 44 and not 49.

No response to the restriction requirement is now necessary in view of the presently pending Petition under 37 C.F.R. § 1.144 with respect thereto.

Claim 54 has been objected to because it depends on non-elected cancelled claim 49.

As discussed above, claim 54 has now been amended to depend from claim 44, thus obviating this objection.

The examiner has objected to the amendment filed on October 16, 2003, under 35 U.S.C. § 132, because it introduces new matter into the specification. The examiner states that the amendments to the specification on pages 13, 14 and 47 are not corrections of an obvious error, but introduce new matter

into the specification. Applicant has been required to cancel the new matter in response to this official action. This objection is respectfully traversed, and reconsideration and withdrawal thereof is respectfully urged.

It is not understood, and the examiner has not explained, why the correction of this error with respect to the definition of "antisense sequence" would not be considered by one of ordinary skill in the art to be an obvious error, particularly in view of the fact that the term was used in the correct and the intended sense elsewhere in the specification, and in view of the dictionary definition of "antisense" and the examiner's own admission.

The language of the original specification at pages 13, 14 and 47, stating, "an oligonucleotide sequence encoding an antisense sequence" is clearly erroneous on its face, since it is well known to anyone of ordinary skill in the art that an antisense sequence is itself an oligonucleotide. An oligonucleotide can only "encode" a peptide. A peptide can never be an antisense sequence. This would have been well known from the dictionary definition of antisense. Note, for example, the attached pages from Stedman's Medical Dictionary, (26th Ed., 1995), where at page 107 it lists "antisense" with the comment, "SEE antisense DNA, antisense RNA." The

definition of "antisense DNA" appears at page 459, where it states:

> the strand of DNA complementary to the one bearing the genetic message and from which it may be reconstructed. A DNA sequence complementary to a portion of mRNA.

The definition of "antisense RNA" appears at page 1549 as follows:

> the transcription product of the DNA antisense strand; it can play a role in the inhibition of translation. SEE ALSO antisense DNA.

Thus, it is clear that antisense is only defined with respect to DNA and RNA sequences, not peptide sequences. See also the attached page 29 of Coombs Dictionary of Biotechnology (2nd Ed., 1992), where it defines antisense as:

> An inverted segment of a specific gene target in a constructed gene. A gene usually produces a message that can be interpreted by a cell (makes 'sense'). The inverted section cannot be interpreted, and is therefore termed 'antisense'. The antisense gene interferes with the function of the targeted gene. Antisense technology is being investigated as a treatment for viral diseases, including cancer and AIDS. It is also applicable in agriculture, bioprocessing and other areas of therapeutics.

Again, it is clear that antisense is a segment of a specific gene target, not a peptide.

This was further noted *sua sponte* by the examiner in the official action of November 5, 2002, at page 5, where she states:

> It is notoriously well known in the art that a triplet codon represents an amino acid. In other words, an oligonucleotide sequence encodes only a peptide sequence, and it does not encodes [sic] an antisense sequence, which is another oligonucleotide sequence.

Thus, the examiner has already conceded on the record that the language "oligonucleotide sequence encoding an antisense sequence" is nonsense, as an antisense sequence must be another oligonucleotide sequence. Thus, the examiner and the dictionary definitions all agree on this point.

As it is clear that this language in the specification as well as in claim 24 as originally filed was clearly erroneous, what, then, was intended? To answer this question, one need only look to other places in the specification. At page 22, line 11, the specification refers to "oligonucleotides having anti-sense B1 sequences." At page 32, lines 10-13, the specification refers to:

> oligonucleotides having the anti-sense coding sequence for the B1 proteins of the invention, which would effectively block the translation of mRNAs encoding the proteins and thereby block their expression and lead to the inhibition of the (cell death) undesired effect.

It is thus clear from pages 22 and 32 that the oligonucleotides, which are considered part of the invention,

are not ones that "encode" an antisense sequence (which the examiner agrees is nonsense as an oligonucleotide sequence cannot encode an antisense sequence), but refers to oligonucleotides having the antisense coding sequence. Thus, the amendment to pages 13, 14 and 47 to change "an oligonucleotide sequence encoding an antisense sequence" to read, "an oligonucleotide sequence which is an antisense sequence" is not new matter, but merely makes these pages correspond to the language used elsewhere in the specification to correct an obvious error, because, as the examiner points out, it is notoriously well known that an oligonucleotide cannot encode an antisense sequence. Accordingly, the fact that there is a defect was clearly obvious to one of ordinary skill in the art, and the correction of the defect is apparent from other portions of the specification. See *In re Oda*, 170 USPQ 268,271(CCPA 1971), where it quotes with approval from *Quigley v. Zimmerman* 23 USPQ 310,314(CCPA 1934), where it stated:

> That amendments may be made to patent applications for the purpose of *curing defects, obvious to one skilled in the art,* in the drawings or written descriptions, is so well settled that we deem it unnecessary to cite authorities in support thereof. [emphasis original]

In that case, the court concluded that there was no new matter, stating at 272:

> On all the evidence, we conclude that one skilled in the art would appreciate not only the existence of error in the specification, but what the error is. As a corollary, it follows that when the nature of this error is known, it is also know how to correct it.

See also MPEP 2163.07 II, where it states:

> An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction.

Such is the case here. One skilled in the art would appreciate not only the existence of the error in the specification, but what the error is, and therefore how to correct it. Accordingly, the correction is not new matter that is objectionable under 35 U.S.C. § 132. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 21 and 51-53 have been rejected under 35 U.S.C. § 112, first paragraph, because they are not supported by subject matter which is described in the specification. This rejection is respectfully traversed.

The language "an oligonucleotide molecule consisting of" is supported by the language "oligonucleotides having anti-sense B1 sequences" at page 22, line 11, and by the language at page 32, lines 10-13. The amendments to the specification at page 13, 14 and 47 are not necessary for

support of claim 24. Nevertheless, these amendments do not contain new matter for the reasons discussed above.

In any event, the amendment has been made to the specification, and with this amendment the specification supports the claims, and therefore of the rejection under 35 U.S.C. § 112, first paragraph, must be withdrawn. The written description requirement says nothing about written description in the specification as originally filed. There must be written description in the specification being examined by the examiner. Amendments to the specification are permissible. If an examiner considers an amendment to the specification to contain new matter, an objection can be made, as the examiner has done. However, the examiner should still consider the subject matter added to the specification when making a written description rejection since the new matter objection may be overcome by applicant. See MPEP 2163.06 I. Thus, until the specification is amended to remove this subject matter, the claims are supported and a rejection under 35 U.S.C. § 112, first paragraph, is inappropriate. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 5-8, 11, 23, 24, 44-48, 51-52 and 54 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement of a DNA sequence encoding a polypeptide analog

or fragment of SEQ ID NO: 1, which analog or fragment potentiates cell death. The examiner correctly summarizes the six points of applicant's argument, but does not specifically respond to each of them. The examiner takes the position that the function of the claimed variants is not predictable when changing the sequence encoding SEQ ID NO: 1 by 2%, because even a single amino acid substitution can dramatically effect the biological activity and characteristics of a protein. The examiner implies that little is known in the prior art about the nature of the invention and the art is unpredictable, and therefore the specification needs more detail as to make and use the invention in order to be enabling. The examiner states that given the unpredictability of protein chemistry, the lack of adequate disclosure in the specification and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undo experimentation to practice the claimed invention. This rejection is respectfully traversed.

Applicant again incorporates by reference the arguments made in the amendment of October 7, 2003, at pages 15-23. The Wands factors have been carefully analyzed and it has been shown that it would not take undue experimentation to practice the claimed invention. While protein chemistry is

somewhat unpredictable, and while it is possible to find a place where a single amino acid change will have a dramatic effect on the biological activity of a protein, this certainly would not be expected for every amino acid. The basic expectation would be that small changes would not dramatically affect the biological activity. Nevertheless, the biological activity can readily be tested by means of assays described in the specification.

The examiner has not explained why it would take undue experimentation to test any given proposed mutein having no more than 10 changes in amino acid sequence to confirm that the biological activity has been maintained. A person of ordinary skill in the art has a high degree of skill, and substantial experimentation is permissible, without such experimentation becoming undue experimentation.

Accordingly, regardless of the fact that protein chemistry is not completely predictable, there is sufficient disclosure in the specification as to the nature and properties of the protein of SEQ ID NO: 1, and assays for determining the activity, to allow one of ordinary skill in the art to readily test any given sequence with fewer than 10 changes in the amino acid sequence thereof, to determine that it has the biological activity of the protein of SEQ ID NO: 1. Accordingly, the claims are in full compliance with the

enablement requirement of 35 U.S.C. § 112. Reconsideration and withdrawal of this rejection are therefore also respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. § 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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antigenicity The ability of a substance to be recognized and bound by a specific antibody.

anti-idiotype antibody An antibody that is induced by, and recognizes, the idiotype of another antibody.

anti-infective A protective agent which reduces the likelihood of disease developing following infection.

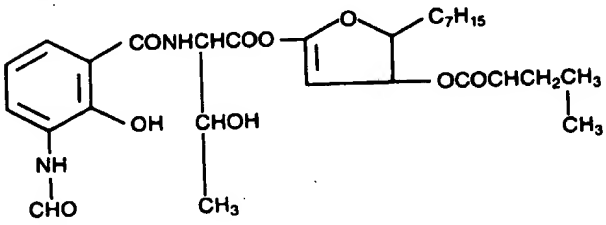
antilymphatic serum Blood serum containing antibodies produced by one species of animal against lymphocytes of another species.

antimetabolite A chemical compound that has a structure similar to a normal metabolic intermediate, but which cannot be metabolized, and so acts as a competitive inhibitor of a specific enzyme reaction.

antimicrobial agent A natural or artificial compound that prevents the growth of or kills microorganisms.

antimutagen A compound that protects against mutations or reverses the effects of mutagens.

antimycin A An antibiotic that blocks hydrogen transport between cytochrome b and cyctochrome c in the mitochondrial respiratory electron transport chain.



Antimycin A

antineoplastic agent A compound that prevents the growth of or kills cancer cells.

antioxidant A substance that inhibits or prevents oxidation.

antisense An inverted segment of a specific gene target in a constructed gene. A gene usually produces a message that can be interpreted by a cell (makes 'sense'). The inverted section cannot be interpreted and is therefore termed 'antisense'. The antisense gene interferes with the function of the targeted gene. Antisense technology is being investigated as a treatment for viral diseases, including cancer and AIDS. It is also applicable in agriculture, bioprocessing and other areas of therapeutics.

antiseptic A chemical compound that is used to destroy organisms that cause infection.

antiserum Whole serum (or the immunoglobulin fraction of blood) containing antibodies from an immunized animal or human. Antiserum containing high levels of antibodies to a specific antigen may be injected to give passive immunity against an infection.

antitermination factor (antiterminator) Specific protein that reacts with a termination signal (nucleotide sequence) to determine whether transcription stops at this site or whether it is read through, thus allowing expression of genes beyond the termination site.

antiterminator *See* antitermination factor.

antitoxin An antibody that reacts with a toxin and neutralizes it.

antitumour agent A compound that reduces the activity or growth of a tumour or cancer cell.

antiviral agent A compound that counteracts viral infections. Interferons are antiviral agents.

AP *See* alkaline phosphatase.

apical dominance The inhibition of the development of lateral buds by the growth of the apical meristem.

apical meristem A region of actively dividing cells that occurs at the tip of roots and shoots.

apocrine secretion The secretion of material by a cell as a result of the loss of part

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tion and thus prevents rancidity of oils or fats or the deterioration of other materials through oxidative processes (*e.g.*, ascorbic acid, vitamin E).

an·ti·pain (an'tē-pā-in). A peptide that inhibits the proteolytic enzymes, papain, trypsin, and plasmin. [*anti-* + p*apain*]

an·ti·par·al·lel (an-tē-par'ă-lel). Denoting molecules that are parallel but point in opposite directions; *e.g.*, the two strands of a DNA double helix.

an·ti·par·a·sit·ic (an'tē-par-ă-sit'ik). Destructive to parasites.

an·ti·pa·ras·ta·ta (an'tē-pa-ras'tă-tă). Obsolete term for bulbourethral *gland*. [anti- + G. *parastatēs*, a testicle]

an·ti·pe·dic·u·lar (an'tē-pe-dik'yū-lăr). Destructive to lice.

an·ti·pe·dic·u·lot·ic (an'tē-pe-dik-yū-lot'ik). Effective in the treatment of pediculosis, especially denoting such an agent.

an·ti·pe·ri·od·ic (an'tē-pēr-ē-od'ik). Preventing the regular recurrence of a disease (*e.g.*, malaria) or a symptom.

an·ti·per·i·stal·sis (an'tē-per-i-stal'sis). SYN reversed *peristalsis*.

an·ti·per·i·stal·tic (an'tē-per-i-stal'tik). **1.** Relating to antiperistalsis. **2.** Impeding or arresting peristalsis.

an·ti·per·spi·rant (an-tē-per'spi-rant). **1.** Having an inhibitory action upon the secretion of sweat. **2.** An agent having such an action (*e.g.*, aluminum chloride). SYN anhidrotic (2). SYN antihidrotic, antihydriotic, antisudorific.

an·ti·phag·o·cyt·ic (an'tē-fag-ō-sit'-ik). Impeding or preventing the action of the phagocytes.

an·ti·phlo·gis·tic (an'tē-flō-jis'tik). **1.** Older term denoting preventing or relieving inflammation. **2.** An agent that reduces inflammation. SYN antipyrotic (1). [anti- + G. *phogistos*, burnt up]

an·ti·pho·bic (an-tē-fō'bik). A mechanism or drug designed to control phobias.

an·ti·plas·min (an-tē-plaz'min). A substance that inhibits or prevents the effects of plasmin; found in plasma and some tissues, especially the spleen and liver. SYN antifibrinolysin.

an·ti·plate·let (an-tē-plāt'let). A substance that manifests a lytic or agglutinative action on the blood platelets, thereby inhibiting or destroying the effects of the latter.

an·ti·pneu·mo·coc·cic (an'tē-nū-mō-kok'sik). Destructive to, or repressing the growth of, the pneumococcus (*e.g.*, penicillin).

an·tip·o·dal (an-tip'ŏ-dăl). Denoting opposite positions; positioned at opposite sides of a cell or other body.

an·ti·pode (an'ti-pōd). That which is diametrically opposite. [G. *antipous*, with the feet opposite]

optical a., SYN enantiomer.

an·ti·port (an'tē-pōrt). The coupled transport of two different molecules or ions through a membrane in opposite directions by a common carrier mechanism (antiporter). Cf. symport, uniport. [anti- + L. *porto*, to carry]

an·ti·por·ter (an'tē-pōr-ter). A protein responsible for mediating the transport of two different molecules or ions simultaneously in opposite directions through a membrane.

an·ti·po·sic (an-tē-pō'sik). Rarely used term for: **1.** Inhibitory to the drinking of water and other beverages. **2.** An agent that has this effect. [anti- + G. *posis*, drinking, + -ic]

an·ti·pre·cip·i·tin (an'tē-prē-sip'i-tin). A specific antibody that inhibits or prevents the effects of a precipitin.

an·ti·pro·ges·tin (an'tē-prō-jes'tin). A substance that inhibits progesterone formation, that interferes with its carriage or stability in the blood, or that reduces its uptake by, or effects on, target organs (*e.g.*, RU-486).

an·ti·pros·tate (an-tē-pros'tāt). Obsolete term for bulbourethral *gland*.

an·ti·pro·throm·bin (an'tē-prō-throm'bin). An anticoagulant that inhibits or prevents the conversion of prothrombin into thrombin; examples are heparin, which is present in various tissues (especially in liver), and dicoumarin, which is isolated from partially decomposed sweet clover.

an·ti·pru·rit·ic (an'tē-prū-rit'ik). **1.** Preventing or relieving itching. **2.** An agent that relieves itching.

an·ti·pso·ric (an-tē-sō'rik). Obsolete term for curative of scabies, or of itching [anti- + G. *psōra*, itch]

an·ti·psy·chot·ic (an'tē-sī-kot'ik). **1.** SYN antipsychotic *agent*. **2.** Denoting the actions of such an agent (*e.g.*, chlorpromazine).

an·ti·pu·rine (an'tē-pyur'ēn). An analog of the purines and purine nucleotides that acts as an antimetabolite.

an·ti·py·o·gen·ic (an'tē-pī-ō-jen'ik). Preventing suppuration. [anti- + G. *pyon*, pus, + *-gen*, production]

an·ti·py·re·sis (an'tē-pī-rē'sis). Symptomatic treatment of fever rather than of the underlying disease.

an·ti·py·ret·ic (an'tē-pī-ret'ik). **1.** Reducing fever. SYN antifebrile, febrifugal. **2.** An agent that reduces fever (*e.g.*, acetaminophen, aspirin). SYN febrifuge. [anti- + G. *pyretos*, fever]

an·ti·py·rim·i·dine (an'tē-pir-im'i-dēn). An analog of the pyrimidines and pyrimidine nucleotides that acts as an antimetabolite.

an·ti·py·rine (an-tē-pī'rin, -pī'rēn). 2,3-Dimethyl-1-phenyl-3-pyrazoline-5-one; an obsolescent analgesic and antipyretic.

a. acetylsalicylate, a compound of a. and aspirin; an antirheumatic and analgesic.

a. salicylacetate, an analgesic, antirheumatic, and antipyretic.

a. salicylate, an analgesic and antipyretic; used in dysmenorrhea, influenza, and acute rhinitis in the early stages.

an·ti·py·rot·ic (an'tē-pī-rot'ik). **1.** SYN antiphlogistic. **2.** Relieving the pain and promoting the healing of superficial burns. **3.** A topical application for burns. [anti- + G. *pyrōtikos*, burning, inflaming]

an·ti·ra·chit·ic (an'tē-ră-kit'ik). Promoting the cure of rickets or preventing its development (*e.g.*, vitamin D preparations).

an·ti·rheu·mat·ic (an'tē-rū-mat'ik). **1.** Denoting an agent which suppresses manifestations of rheumatic disease; usually applied to anti-inflammatory agents or agents that are capable of delaying progression of the basic disease process in inflammatory arthritis. **2.** An agent possessing such properties (*e.g.*, gold compounds).

an·ti·ri·cin (an-tē-rī'sin). An antibody or antitoxin that inhibits or prevents the effects of ricin.

an·ti·ru·mi·nant (an-tē-rū'mi-nănt). Denoting a method to 1) control regurgitation of food or 2) break a compulsive trend of thought. [anti- + L. *rumino*, to chew the cud, fr. *rumen*, throat]

an·ti-S. See MNSs blood group, Blood Groups appendix.

an·ti·scor·bu·tic (an'tē-skōr-byū'tik). **1.** Preventive or curative of scurvy (scorbutus). **2.** A treatment for scurvy (*e.g.*, vitamin C).

an·ti·seb·or·rhe·ic (an'tē-seb-ō-rē'ik). **1.** Preventing or relieving excessive secretion of sebum; preventing or relieving seborrheic dermatitis. **2.** An agent having such actions.

an·ti·se·cre·to·ry (an'tē-sē-krē'tō-rĭ). Inhibitory to secretion, said of certain drugs that reduce or suppress gastric secretion (*e.g.*, ranitidine, omeprazole).

an·ti·sense (an'tē-sens). SEE antisense DNA, antisense RNA.

an·ti·sep·sis (an-tē-sep'sis). Prevention of infection by inhibiting the growth of infectious agents. SEE ALSO disinfection. [anti- + G. *sēpsis*, putrefaction]

an·ti·sep·tic (an-tē-sep'tik). **1.** Relating to antisepsis. **2.** An agent or substance capable of effecting antisepsis.

an·ti·se·rum (an-tē-sē'rŭm). Serum that contains demonstrable antibody or antibodies specific for one (monovalent or specific a.) or more (polyvalent a.) antigens; may be prepared from the blood of animals inoculated parenterally (under certain conditions) with an antigenic material or from the blood of animals and persons that have been stimulated by natural contact with an antigen (as in those who recover from an attack of disease). SYN immune serum.

blood group a.'s, see Blood Groups appendix.

heterologous a., an a. that reacts with (*e.g.*, agglutinates) certain microorganisms or other complexes of antigens, even though the a. was produced by means of stimulation with a different microorganism or antigenic material. SEE ALSO homologous a.

homologous a., an a. in which there is complete correspondence between the content of antibodies and the antigenic material used for producing the a.

monovalent a., SEE antiserum.

nerve growth factor a., an a. containing antibodies against

Under appropriate conditions, it can produce single-strand nicks in DNA; used in nick translation and in the mapping of hypersensitive sites. SYN pancreatic d., thymonuclease.

d. II, DNase II, an endonuclease that cleaves both strands of native DNA (as well as single-stranded DNA) to produce a mixture of oligodeoxynucleotides, each ending in a 3′-phosphate. SYN acid d.

pancreatic d., SYN d. I.

d. S_1, SYN endonuclease S_1 *Aspergillus*.

spleen d., former name for micrococcal *endonuclease*.

de·ox·y·ri·bo·nu·cle·ic ac·id (DNA) (dē-oks′ē-rī′bō-nū-klē′ik). The type of nucleic acid containing deoxyribose as the sugar component and found principally in the nuclei (chromatin, chromosomes) and mitochondria of animal and vegetable cells, usually loosely bound to protein (hence the term deoxyribonucleoprotein); considered to be the autoreproducing component of chromosomes and of many viruses, and the repository of hereditary characteristics. Its linear macromolecular chain consists of deoxyribose molecules esterified with phosphate groups between the 3′ and 5′ hydroxyl groups; linked to this structure are the purines adenine (A) and guanine (G) and the pyrimidines cytosine (C) and thymine (T). DNA may be open-ended or circular, single- or double-stranded, and many forms are known, the most comonly described of which is double-stranded, wherein the pyrimidines and purines cross-link through hydrogen bonding in the schema A-T and C-G, bringing two antiparallel strands into a double helix. Chromosomes are composed of double-stranded DNA; mitochondrial DNA is circular.

A-DNA, a form of DNA in which the helix is right-handed and the overall appearance is short and broad.

antisense DNA, the strand of DNA complementary to the one bearing the genetic message and from which it may be reconstructed. A DNA sequence complementary to a portion of mRNA.

B-DNA, a form of DNA in which the helix is right-handed and the overall appearance is long and thin.

blunt-ended DNA, double-stranded DNA in which at least one of the ends has no unpaired bases.

competitor DNA, DNA from a test organism that is denatured and then used in *in vitro* hybridization experiments in which it competes with DNA (homologous) from a reference organism; used to determine the relationship of the test organism to the reference organism.

complementary DNA (cDNA), (1) single-stranded DNA that is complementary to messenger RNA; (2) DNA that has been synthesized from mRNA by the action of reverse transcriptase.

extrachromosomal DNA, DNA that occurs naturally outside of the nucleus (*e.g.,* mitochondrial DNA).

genomic DNA, DNA that contains both introns and exons.

junk DNA, that portion of DNA which is not transcribed and expressed, comprising about 90% of the 3 billion base pairs of the human genome; its function is not known.

DNA ligase, an enzyme that leads to the formation of a phosphodiester bond at a break of one strand in duplex DNA; a part of the DNA repair system.

linker DNA, the DNA found between nucleosomes on chromatin; since it is not complexed to proteins as strongly as other forms of DNA, it is accessible to exonuclease hydrolysis.

DNA nucleotidylexotransferase, an enzyme that can catalyze the addition of a nucleotide, presented as a nucleoside triphosphate, on a DNA or similar polydeoxynucleotide; has been used in DNA recombination studies to add nucleotides to form homopolymer tails. SYN terminal addition enzyme, terminal deoxynucleotidyltransferase.

palindromic DNA, a segment of DNA in which the sequence is symmetrical about its midpoint.

DNA polymerase, SEE nucleotidyltransferases.

recombinant DNA, SEE recombinant DNA.

repetitive DNA, a segment of DNA that consists of a linear array of multiple copies of the same sequence of nucleotides.

satellite DNA, DNA in the satellite regions of acrocentric chromosomes.

sticky-ended DNA, double-stranded DNA in which one of the strands protrudes from the other strand (*i.e.,* has a number of unpaired bases) at one end or more.

Z-DNA, a form of DNA in which the helix is left-handed, and the overall appearance is elongated and slim.

zero time-binding DNA, DNA that has become the duplex form at the start of a reassociation process.

de·ox·y·ri·bo·nu·cle·o·pro·tein (DNP, Dnp) (dē-oks′ē-rī-bō-nū′klē-ō-prō′tēn). The complex of DNA and protein in which DNA is usually found upon cell disruption and isolation.

de·ox·y·ri·bo·nu·cle·o·side (dē-oks′ē-rī-bō-nū′klē-ō-sīd). A nucleoside component of DNA containing 2-deoxy-D-ribose; the condensation product of deoxy-D-ribose with purines or pyrimidines.

de·ox·y·ri·bo·nu·cle·o·tide (dē-oks′ē-rī-bō-nū′klē-ō-tīd). A nucleotide component of DNA containing 2-deoxy-D-ribose; the phosphoric ester of deoxyribonucleoside; formed in nucleotide biosynthesis.

de·ox·y·ri·bose (dē-oks-ē-rī′bōs). A deoxypentose, 2-deoxy-D-ribose being the most common example, occurring in DNA and responsible for its name.

d. phosphate, SEE deoxyribonucleotide.

de·ox·y·ri·bose·phos·phate al·dol·ase (dē-oks′ē-rī-bōs-fos′fāt). An enzyme catalyzing cleavage of 2-deoxy-D-ribose 5-phosphate to D-glyceraldehyde 3-phosphate and acetaldehyde. SYN deoxyriboaldolase.

de·ox·y·ri·bo·side (dē-oks-ē-rī′bō-sīd). Deoxyribose combined via its 1-O atom with a radical derived from an alcohol; not to be confused with deoxyribosyl compounds such as deoxyribonucleosides. Cf. deoxyribosyl.

de·ox·y·ri·bo·syl (dē-oks-ē-rī′bō-sil). The radical formed from deoxyribose by removal of the OH from the C1 carbon; *e.g.,* deoxyadenosine. Cf. deoxyriboside.

de·ox·y·ri·bo·syl·trans·fer·ases (dē-oks′ē-rī′bō-sil-trans′fer-ās-es). Enzymes that catalyze the transfer of 2-deoxy-D-ribose from deoxyribosides to free bases.

de·ox·y·ri·bo·tide (dē-oks-ē-rī′bō-tīd). Misnomer for deoxyribonucleotide or deoxynucleotide derived, by analogy with nucleoside-nucleotide, from incorrect usage of deoxyriboside.

de·ox·y·thy·mi·dine (dT) (dē-oks′ē-thi′mi-dēn). SYN thymidine.

de·ox·y·thy·mi·dyl·ic ac·id (dTMP) (dē-oks′ē-thī-mi-dil′ik). A component of DNA; originally and properly called thymidylic acid, but use of deoxy- is less ambiguous, as ribothymidylic acid is now known to exist. SYN thymine deoxyribonucleotide.

de·ox·y·ur·i·dine (dē-oks′ē-yūr′i-dēn). A derivative of uridine in which one or more of the hydroxyl groups on the ribose moiety has been replaced by a hydrogen; *e.g.,* 2′-deoxyuridine is a rare naturally occurring deoxynucleoside.

de·ox·y·vi·rus (dē-ok′sē-vī′rŭs). SYN DNA *virus*.

de·o·zon·ize (dē-ō′zō-nīz). To deprive of ozone.

de·pen·dence (dē-pen′dens). The quality or condition of relying upon, being influenced by, or being subservient to a person or object reflecting a particular need. [L. *dependeo,* to hang from]

anchorage d., the need of normal cells to have an appropriate surface to attach to in order for them to grow in culture.

substance d., a pattern of behavioral, physiologic, and cognitive symptoms that develop due to substance use or abuse; usually indicated by tolerance to the effects of the substance and withdrawal symptoms that develop when use of the substance is terminated.

de·pen·den·cy (dē-pen′dens-ē). The state of being dependent.

pyridoxine d. with seizure, an inherited disorder (autosomal recessive) apparently associated with deficient brain type I glutamate decarboxylase; seizures can be controlled with vitamin B_6.

De·pen·do·vi·rus (dē-pen′dō-vī-rŭs). A genus of small defective single-stranded DNA viruses in the family Parvoviridae that depend on adenoviruses for replication. SYN adeno-associated virus, adenosatellite virus. [L. *dependeo,* to be dependent upon, + virus]

de·per·son·al·i·za·tion (dē-per′sŏn-ăl-i-zā′shŭn). A state in which a person loses the feeling of his own identity in relation to

ri·bo·fla·vin, ri·bo·fla·vine (rī′bō-flā-vin). 7,8-dimethyl-10-(1′-D-ribityl)isoalloxazine; a heat-stable factor of the vitamin B complex whose isoalloxazine nucleotides are coenzymes of the flavodehydrogenases. The daily human requirement is 1.7 mg for adult men and 1.3 mg for adult women, with a higher daily requirement during pregnancy and lactation; dietary sources include green vegetables, liver, kidneys, wheat germ, milk, eggs, cheese, and fish. SYN flavin (1), flavine, lactoflavin (2), vitamin B_2 (1).

r. kinase, a cytosolic enzyme catalyzing the formation of flavin mononucleotide (r. phosphate) from r., utilizing ATP as phosphorylating agent. SYN flavokinase.

r. methylol r., a mixture of methylol derivatives of r. formed by the reaction of formaldehyde on r. in weakly alkaline solution; it has the same action as r., but is preferred for parenteral administration.

ri·bo·fla·vin 5′-phos·phate. SYN *flavin* mononucleotide.

ri·bo·fu·ra·nose (rī-bō-fūr′ă-nōs). The 1,4 cyclic furan form of ribose.

9-β-D-ri·bo·fu·ran·o·syl·ad·e·nine (rī′bō-fūr-an′o-sil-ad′ĕ-nēn). SYN adenosine.

1-β-D-ri·bo·fu·ran·o·syl·cy·to·sine (rī′bō-fūr-an′o-sil-sī′tō-sēn). SYN cytidine.

9-β-D-ri·bo·fu·ran·o·syl·gua·nine (rī′bō-fūr-an′ō-sil-gwah′nēn). SYN guanosine.

9-β-ribofuranosylpurine. SYN nebularine.

ri·bo·fu·ran·o·syl·thy·mine (rī′bō-fūr-an′ō-sil-thī′mēn). SYN ribothymidine.

1-β-D-ri·bo·fu·ran·o·syl·u·ra·cil (rī′bō-fūr-an′ō-sil-yūr′ă-sil). SYN uridine.

ri·bo-2-hex·u·lose. SYN psicose.

ri·bo·nu·cle·ase (RNase) (rī-bō-nū′klē-ās). A transferase or phosphodiesterase that catalyzes the hydrolysis of ribonucleic acids. SEE ALSO ribonuclease (pancreatic), ribonuclease (*Bacillus subtilis*). SYN ribonucleinase.

r. A, ribonuclease (pancreatic).

alkaline RNase, ribonuclease (pancreatic).

RNase alpha, an enzyme catalyzing endonucleolytic cleavage of 2′-methylated RNA yielding 5′-phosphomonoesters.

r. D (RNase D), an enzyme (endonuclease) that trims the extra 3′-nucleotides from immature tRNA.

***Escherichia coli* RNase I,** SYN RNase T_2.

RNase I, ribonuclease (pancreatic).

RNase II [EC 3.1.13.1], an enzyme cleaving RNA exonucleolytically in the 3′ to 5′ direction, yielding 5′-phosphomononucleotides. SEE ALSO microbial RNase II.

RNase III, an enzyme catalyzing endonucleolytic cleavage of double-stranded RNA yielding 5′-phosphomonoesters.

microbial RNase II, SYN RNase T_2.

RNase N_1, SYN RNase T_1.

RNase N_2, SYN RNase T_2.

RNase P, an enzyme catalyzing the endonucleolytic cleavage tRNA precursors to yield 5′-phosphomonoesters.

r. P (RNase P), an enzyme (endonuclease) that trims the extra 5′ nucleotides from immature tRNA; a protein RNA complex.

pancreatic RNase, SEE ribonuclease (pancreatic).

plant RNase, SYN RNase T_2.

RNase T_1, a nuclease endonucleolytically cleaving ribonucleic acids at the 3′-5′ link of a guanosine 3′-phosphate residue, producing oligonucleotides terminating in this nucleotide; a transferase (endonuclease) in the first (cyclizing) step, a phosphodiesterase on the second (hydrolyzing) step. SYN guanyloribonuclease, RNase N_1.

RNase T_2, an enzyme endonucleolytically cleaving RNA to 3′-nucleotides with 2′,3′-cyclic nucleotides as intermediates. SYN *Escherichia coli* RNase I, microbial RNase II, plant RNase, RNase N_2.

RNase U_2, an enzyme endonucleolytically cleaving RNA to 3′-phospho-mono- and oligonucleotides ending in adenylate or guanylate residues with 2′,3′-cyclic phosphate intermediates.

RNase U_4, SYN yeast RNase.

yeast RNase, an enzyme catalyzing the exonucleolytic cleavage of RNA to yield 3′-phosphomononucleotides. SYN RNase U_4.

ri·bo·nu·cle·ase (*Ba·cil·lus sub·ti·lis*). 1. Ribonuclease (*Azotobacter agilis*); ribonuclease (*Proteus mirabilis*); an enzyme catalyzing the endonucleolytic cleavage of RNA to yield 2′,3′-cyclic nucleotides. **2.** Ribonuclease T_1.

ri·bo·nu·cle·ase (pan·cre·at·ic). An enzyme that transfers the 3′-phosphate of a pyrimidine ribonucleotide residue in a polynucleotide from the 5′-position of the adjoining nucleotide to the 2′-position of the pyrimidine nucleotide itself (a transferase, endonuclease action), thus breaking the chain and forming a pyrimidine 2′,3′-cyclic phosphate, then (or independently) hydrolyzing this phosphodiester to leave a pyrimidine nucleoside 3′-phosphate residue (phosphodiesterase action); used in cytochemistry to selectively degrade and remove RNA as a control for staining of RNA.

ri·bo·nu·cle·ic ac·id (RNA) (rī′bō-nū-klē′ik). A macromolecule consisting of ribonucleoside residues connected by phosphate from the 3′-hydroxyl of one to the 5′-hydroxyl of the next nucleoside. RNA is found in all cells, in both nuclei and cytoplasm and in particulate and nonparticulate form, and also in many viruses; polynucleotides made *in vitro* are generally called such. Various RNA fractions are identified by location, form, or function.

acceptor RNA, SYN transfer RNA.

antisense RNA, the transcription product of the DNA antisense strand; it can play a role in the inhibition of translation. SEE ALSO antisense DNA.

chromosomal RNA, RNA associated with the chromosome (not mRNA, tRNA, or rRNA) that may have a role in transcription.

heterogeneous nuclear RNA (hnRNA), an ill-defined form of RNA, of high molecular weight, that never leaves the nucleus and is thought to be the precursor of messenger RNA.

informational RNA, SYN messenger RNA.

initiation tRNA, tRNA in prokaryotes containing a formyl-methionyl residue that initiates translation. SYN formyl-methionyl-tRNA, starter tRNA.

messenger RNA (mRNA), the RNA reflecting the exact nucleoside sequence of the genetically active DNA and carrying the "message" of the latter, coded in its sequence, to the cytoplasmic areas where protein is made in amino acid sequences specified by the mRNA, and hence primarily by the DNA; viral RNA's are considered to be natural messenger RNA's. SYN informational RNA, template RNA.

messenger-like RNA (mlRNA), SEE heterogeneous nuclear RNA.

nuclear RNA (nRNA), rNA found in nuclei, or associated with DNA, or with nuclear structures (nucleoli).

RNA polymerase, SEE nucleotidyltransferases.

ribosomal RNA, the RNA of ribosomes and polyribosomes.

small nuclear RNA (snRNA), small RNA, *i.e.,* about 90 to 300 nucleotides long in the nucleus believed to have a role in RNA processing and cellular architecture.

soluble RNA (sRNA), SYN transfer RNA. [soluble in molar salt]

starter tRNA, SYN initiation tRNA.

suppressor tRNA, the tRNA associated with a suppressor mutation.

template RNA, SYN messenger RNA.

transfer RNA (tRNA), short-chain RNA molecules present in cells in at least 20 varieties, each variety capable of combining with a specific amino acid (see aminoacyl-tRNA). By joining (through their anticodons) with particular spots (codons) along the messenger RNA molecule and carrying their amino acyl residues along, they lead to the formation of protein molecules with a specific amino acid arrangement—the one ultimately dictated by a segment of DNA in the chromosomes. Each tRNA has about 80 nucleotides (MW about 25,000); most of the 20 varieties occur in multiple "isoacceptor" forms, separable by chromatography. Further subvarieties exist in different strains of an organism, in subcellular organelles, in different metabolic states, etc. Cognate tRNA's are the tRNA's recognized by the specific amino acyl-tRNA synthetases. SYN acceptor RNA, soluble RNA.

ri·bo·nu·cle·i·nase (rī-bō-nū′klē-i-nās). SYN ribonuclease.